REMARKS

Claim Amendments

Claims 1-13, 15-22, 24-31, 34, and 35 are currently pending. Claims 15, 16, 24, 25, 34, and 35 are allowed. Claims 14, 23, 32, and 33 were previously canceled without prejudice. Claims 8-13,17, 19 and 26-30 have been canceled without prejudice with this response. Claims 1, 2, 4, 5, 18-20, and 31 have been amended with this response.

Claim 1 has been amended to recite a method of identifying a candidate branching morphogenesis modulating agent comprising the steps of: (1) providing a first assay system capable of detecting mitogen-activated protein kinase kinase 6 (MAP2K6) expression or activity comprising a MAP2K6 polypeptide or nucleic acid; (2) contacting the assay system of step (a) with a candidate test agent; (3) measuring the expression or activity of MAP2K6 in the presence or absence of the test agent; (4) identifying a candidate branching morphogenesis modulating agent by detecting a change in the expression or activity of MAP2K6 in the presence of the test agent compared with no test agent; (5) providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells or a non-human animal expressing MAP2K6; (6) contacting the assay system of step (e) with the candidate test agent of (b); (7) measuring the branching morphogenesis pathway in the presence or absence of the test agent; and (8) confirming that the test agent of (b) is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent. Support for the amendment can be found in the specification at, for example, pages 3, 4, and 21-34.

Claims 2, 4, and 5 have been amended to clarify that the recited assay system refers to the first assay system. Support for the amendments can be found in the specification at, for example, pages 4 and 21-31.

Claims 18 and 20 have been amended to correct their dependencies and to clarify that the second assay system includes an assay that detects a change or event from a specified assay. Support for these amendments are found in the specification at, for example, pages 4 and 31-34.

Claim 31 has been amended to recite a method for diagnosing prostate, stomach, or testis cancer in a patient comprising: (a) obtaining a biological sample from the prostate, stomach, or testis of a cancer patient; (b) contacting the biological sample in step (a) with a probe for MAP2K6 expression; (c) contacting a tissue-matched control sample with a probe for MAP2K6 expression; (d) detecting an elevated level of MAP2K6 expression in the biological sample of step (b) compared with the tissue-matched control sample of step (c); and (e) determining whether step (d) indicates a likelihood of prostate, stomach, or testis cancer. Support for these amendments are found in the specification at, for example, pages 36 and 40-42.

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections. Additionally, these amendments are not an admission regarding the patentability of subject matter of the canceled or amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application.

Allowed Claims

Applicants gratefully acknowledge the allowance of Claims 15, 16, 24, 25, 34, and 35.

35 USC §102 Rejections

Claims 1, 31 and 32 have been rejected under 35 USC §102(b) as being allegedly anticipated by Wong et al (Gynecologic Oncology, 2001, 82:305-311). Claim 32 was previously canceled. Applicants respectfully traverse the rejections of claim 1 and 31 for the reasons set forth below.

Under 35 U.S.C. § 102(b), a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.,* 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); M.P.E.P § 2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.,* 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); M.P.E.P. § 2131. Furthermore, the prior art reference must provide an enabling disclosure. M.P.E.P. §2121.01; *In re Hoeksema,* 399 F.2d 269 (CCPA 1968) ("In

determining that quantum of prior art disclosure which is necessary to declare an applicant's invention' 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... .").

The Office argued that the Wong et al. reference anticipates claims 1 and 31 because it discloses a method of measuring the expression level of MAP2K6 polynucleotides in normal, pre-neoplastic, and neoplastic ovarian cell lines and ovarian surface epithelial cells obtained from patients in the presence and absence of hepatocyte growth factor (ie, a test agent). The Office did not accord the phrases a method "of identifying a candidate branching morphogenesis modulating agent" and a method "for diagnosing a disease in a patient" any patentable weight because the phrases occur in the preamble. In addition, the Office did not give the phrase "wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent" any patentable weight and also did not give steps (c) and (d) any patentable weight as they are allegedly confined to mental steps rather than to active method steps.

Applicants strongly disagree with the Office's characterization of the claims in that the preamble, wherein clause, and the method steps do not carry patentable weight for all of the reasons set forth in the previous response filed on March 23, 2009 (not repeated here).

However, in an effort to expedite prosecution, the Applicants have amended the claims. To anticipate claim 1 as amended, the Wong et al reference must teach a method of identifying a candidate branching morphogenesis modulating agent comprising the steps of: (a) providing a first assay system capable of detecting MAP2K6 expression or activity comprising a MAP2K6 polypeptide or nucleic acid; (b) contacting the assay system of step (a) with a candidate test agent; (c) measuring the expression or activity of MAP2K6 in the presence or absence of the test agent; (d) identifying a candidate branching morphogenesis modulating agent by detecting a change in the expression or activity of MAP2K6 in the presence of the test agent compared with no test agent; (e) providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6; (f) contacting the assay system of step (e) with the candidate test agent of (b); (g) measuring the

branching morphogenesis pathway in the presence or absence of the test agent; and (h) confirming that the test agent of (b) is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

The Wong et al reference fails to anticipate claim 1 as amended because it fails to teach each and every element as set forth in the claims. Specifically, the Wong et al. reference fails to recognize the connection between MAP26 and the branching morphogenesis pathway and thus fails to teach a method comprising steps (e) - (h) of the claimed method. Therefore, Wong et al. fails to teach each and every step of the claimed invention and thus fails to anticipate claim 1.

To anticipate claim 31 as amended, the Wong et al reference must teach a method for diagnosing liver, prostate, skin, stomach, or testis cancer in a patient comprising: (a) obtaining a biological sample from the prostate, stomach, or testis of a cancer patient; (b) contacting the biological sample in step (a) with a probe for MAP2K6 expression; (c) contacting a tissue-matched control sample with a probe for MAP2K6 expression; (d) detecting an elevated level of MAP2K6 expression in the biological sample of step (b) compared with the tissue-matched control sample of step (c); and (e) determining whether step (d) indicates a likelihood of prostate, stomach, or testis cancer.

Wong et al. measures the expression level of MAP2K6 polynucleotides in normal, pre-neoplastic, and neoplastic ovarian cell lines and ovarian surface epithelial cells obtained from patients with ovarian cancer. Thus, Wong et al. fails to teach or suggest a method for diagnosing prostate, stomach, or testis cancer in a patient comprising, among other things, obtaining a biological sample from the prostate, stomach, or testis of a cancer patient (step (a)). Wong et al. also fails to teach steps (d) detecting an elevated level of MAP2K6 expression in the biological sample from the prostate, stomach, or testis of a cancer patient compared with the tissue-matched control sample of step (c); and (e) determining whether step (d) indicates a likelihood of prostate, stomach, or testis cancer.

The Wong et al reference fails to anticipate claim 31 as amended because it fails to teach each and every element as set forth in the claims. Specifically, the Wong et al. reference fails to recognize the connection between MAP26 and prostate, stomach, and

testis cancer and thus fails to teach a method comprising steps (a) - (e) of the claimed method. Therefore, Wong et al. fails to teach each and every step of the claimed invention and thus fails to anticipate claim 31.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §102(b) rejections in view of Wong et al.

Claims 1-6, 17, 19, and 26-30 were rejected under 35 USC §102(b) as being allegedly anticipated by Stein et al (W097/22704). Claims 17, 19 and 26-30 have been canceled, rendering the rejections moot as to these claims. Applicants respectfully traverse the rejections with respect to claims 1-6 for the reasons set forth below.

The Office argued that the Stein et al. reference anticipates claims 1-6 because it discloses a method for identifying a composition which affects MAP2K6 activity comprising incubating the composition and MEK6 kinase or polynucleotide encoding the kinase and measuring the effect of the composition on the MEK6 kinase protein or polynucleotide as well as disclosing a second assay system comprising a kinase assay to measure the activity of p38 in response to MEK6. The Office did not accord the phrases a method "of identifying a candidate branching morphogenesis modulating agent" and "wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent" any patentable weight.

Applicants strongly disagree with the Office's characterization of the claims in that the preamble and wherein clause do not carry patentable weight for all of the reasons set forth in the previous response filed on March 23, 2009 (not repeated here).

However, in an effort to expedite prosecution, the Applicants have amended the claims. To anticipate claim 1 (and claims dependent thereon) as amended, the Stein et al reference must teach a method of identifying a candidate branching morphogenesis modulating agent comprising the steps of: (a) providing a first assay system capable of detecting MAP2K6 expression or activity comprising a MAP2K6 polypeptide or nucleic acid; (b) contacting the assay system of step (a) with a candidate test agent; (c) measuring the expression or activity of MAP2K6 in the presence or absence of the test agent; (d) identifying a candidate branching morphogenesis modulating agent by detecting a change in the expression or activity of MAP2K6 in the presence of the test agent compared with

no test agent; (e) providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6; (f) contacting the assay system of step (e) with the candidate test agent of (b); (g) measuring the branching morphogenesis pathway in the presence or absence of the test agent; and (h) confirming that the test agent of (b) is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

The Stein et al reference fails to anticipate the present claims because it fails to teach each and every element as set forth in the claims. The Stein et al. reference is directed to compositions and methods for potentiating the activity of p38 using MEK6 (MAP2K6). Stein et al teaches contacting a candidate agent with a MEK6 polypeptide and subsequently measuring the ability of the MEK6 polypeptide to activate p38. In contrast to the present invention, the Stein et al. reference fails to even contemplate a method for identifying a candidate branching morphogenesis modulating agent using an assay system comprising MAP2K6 polypeptide or nucleic acid, much less teach or suggest such method. Therefore, Stein et al. fails to teach at least steps (e)- (g).

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §102(b) rejections in view of Stein et al.

Claims 1, 26-28, 30, and 31 were rejected under 35 USC §102(b) as being allegedly anticipated by Davis et al (W096/36642). Claims 26-28, and 30 have been canceled, rendering the rejections moot as to these claims. Applicants respectfully traverse the rejections with respect to claims 1 and 31 for the reasons set forth below.

To anticipate claim 1 as amended, the Stein et al reference must teach a method of identifying a candidate branching morphogenesis modulating agent comprising, among other steps, the steps of: (e) providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6; (f) contacting the assay system of step (e) with the candidate test agent of (b); (g) measuring the branching morphogenesis pathway in the presence or absence of the test agent; and (h) confirming that the test agent of (b) is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

The Davis et al reference fails to anticipate claim 1 because it fails to teach each and every element as set forth in the claims. The Davis et al. reference is directed to MKK polypeptides and polynucleotides (including MKK6 or MAP2K6). Davis et al suggests that MKK polypetides and polynucleotides can be useful to screen reagents that modulate MKK synthesis or activity. However, Davis et al. fail to mention branching morphogenesis and therefore fail to even contemplate a method for identifying a candidate branching morphogenesis modulating agent using a first assay system comprising MAP2K6 polypeptide or nucleic acid and a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6, much less teach or suggest such a method. Therefore, Davis et al. fails to teach at least steps (e)- (g) of claim 1.

The Office argued that Davis et al. disclose a method of identifying a subject at risk for a Map kinase disorder by measuring activation of the MKK signal pathway and disclose that MKK-mediated disorders include various malignancies of the skin and liver. Applicants submit that while Davis et al. generally disclose that MKK synthesis can be used to identify a subject at risk for a Map kinase disorder, it does not teach a specific method for doing so and therefore fails to teach each and every step of claim 31. However, in an effort to expedite prosecution, Applicants have amended claim 31 to delete reference to liver and skin cancer. Davis et al. does not teach or suggest that MKK can be used to identify a subject at risk for prostate, stomach, or testis cancer. Therefore, Davis et al. fails to teach the method of claim 31.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §102(b) rejections in view of Davis et al.

35 USC §103 Rejections

Claims 1-6, 17, 19, and 20 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704). Claims 17 and 19 have been canceled, rendering the rejections moot as to those claims. Applicants respectfully traverse the rejections of claims 1-6 and 20 for the reasons set forth below.

The Office Action alleged that Stein et al. teach the MEK6 assay coupled with the p38 assay. The Office argued that while Stein et al. do not specifically teach an assay that would measure cell proliferation and cell cycling, it would have been obvious to one skilled in the art to use an assay which would measure alterations in cell proliferation and cell cycling in conjunction with the second p38 assay. The Office alleged that one skilled in the art would have been motivated to do so because Stein e al. teach that the diseases associated with the p38 cascade include cell-growth related diseases such as cancer, abnormal cell growth and proliferation and cell cycle abnormalities. The Office concluded that one skilled in the art would have understood from the teachings of Stein et al. that modulation of cell proliferation and cell cycling can result from modulation of p38 activity as a result of modulation of MEK6 activity.

Applicants submit that Stein et al do not render obvious the claimed invention. A claimed invention is unpatentable if the differences between it and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a); *see Graham v. John Deere Co.*, 383 U.S. 1, 14 (1966). The ultimate determination of whether an invention is or is not obvious is based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. *See Graham, 383 U.S. at 17-18.*

To meet the requirements for *prima facie* case of obviousness, the Office must demonstrate that the references teach or suggest all the limitations of the claims. Post-KSR, the Board of Patent Appeals and Interferences (BPAI) has continued to maintain that

> [A]n examiner must make "a searching comparison of the claimed invention — *including all its limitations* - with the teaching of the prior art." *In re Ochiai,* 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis added). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.,* 349 F.3d, 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka,* 490 F.2d 981, 985 (CCPA 1974)). *Ex Parte* Wada, BPAI, Appeal 2007-377, page 7 (Jan. 15, 2008) (unpublished).

See also, Ex parte Shepard, BPAI, Appeal 2008-0401, page 7 (Jan. 3, 2008) (unpublished) (BPAI reversed the Examiner's rejection of obviousness, because "having failed to demonstrate that the references teach the limitations of claim 11, the Examiner failed to establish a *prima facie* case of obviousness for claims 17 or 18 which depend from claim 11.").

As discussed in detail above, Stein et al. fail to teach all of the elements of the claimed methods of identifying a candidate branching morphogenesis modulating agent as required to establish a *prima facie* case of obviousness. Specifically, Stein et al. fails to teach or suggest a method of identifying a candidate branching morphogenesis modulating agent comprising providing a first assay system capable of detecting MAP2K6 expression or activity comprising a MAP2K6 polypeptide or nucleic acid and measuring the expression or activity of MAP2K6 in the presence or absence of the test agent to identify a candidate branching morphogenesis modulating agent and providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6, measuring the branching morphogenesis pathway in the presence or absence of the test agent and confirming that the test agent is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

The Supreme Court has emphasized that the key in supporting any rejection under 35 U.S.C. §103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). The Court, quoting *In re Kahn*, stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441, F.3d 977, 988 (Fed. Cir. 2006).

In this case, the Office has failed to clearly articulate the reason(s) why the claimed invention would have been obvious over the teachings of Stein et al. Applicants submit that Stein et al provides no teaching whatsoever of branching morphogenesis or the modulation thereof. Thus, Stein fails to teach or suggest a

link between MAP2K6 and branching morphogenesis modulation and also fails to teach or suggest a connection between p38 and branching morphogenesis modulation. In the absence of any teaching whatsoever of a connection between MAP2K6 or p38 and branching morphogenesis modulation, one skilled in the art simply would not have been motivated to pursue a method of identifying a candidate branching morphogenesis modulating agent using a first assay system comprising MAP2K6 polypeptide or nucleic acid and a second assay system comprising cultured cells expressing MAP2K6 that detects an agent-biased change in the branching morphogenesis pathway, much less have a reasonable expectation of successfully applying such method.

With respect to claim 20, the Office admitted that Stein et al do not teach using an assay that measures cell proliferation or cell cycling; however, it alleged that it would have been obvious to use an assay that measures alterations in cell proliferation or cell cycling based on the teachings in Stein et al relating to the diseases associated with the p38 cascade. However, the only assay taught by Stein et al for use in identifying candidate modulating agents is a kinase assay to measure the activity of MEK6 and subsequently the activity of p38. Stein et al. only briefly mention disease conditions associated with p38 in the completely unrelated context of using modulating agents for therapeutic purposes. Stein et al make no mention of p38 associated diseases in the context of assays used for identifying MEK6 or p38 modulating agents and therefore provide no motivation whatsoever to use an assay that would measure alterations in cell proliferation or cell cycling in a method for identifying candidate modulating agents comprising steps (a) – (h).

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al.

Claims 1-6, 8-11, and 17-20 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Sodhi et al (Cancer Research, 2000, 60:4873-4880). Claims 8-11, 17, and 19 have been canceled, rendering the rejections moot as to those claims. Applicants respectfully traverse the rejections of claims 1-6, 18, and 20 for the reasons set forth below.

The Office indicated that Stein et al. renders obvious the detection of modulation in cell proliferation and cell cycling as a result of modulation of p38 resulting from the

modulation of MEK6 for the reasons previously stated. With respect to claims 18 and 20, the Office admitted that Stein et al do not teach or suggest an assay that detects an event which is a response to hypoxic conditions or angiogenesis. However, the Office asserted that one skilled in the art would have been motivated to use such an assay based on the teachings of Sodhi et al which allegedly teach that both the MAPK and p38 pathways act by modulating the phosphorylation state of HIF-1 in response to hypoxic conditions which results in the upregulation of VEGF and subsequent angiogenesis.

Applicants submit that Stein et al do not teach or suggest a method of identifying a candidate branching morphogenesis modulating agent for the reasons previously discussed. Specifically, Stein et al. do not teach or suggest a method comprising providing a first assay system capable of detecting MAP2K6 expression or activity comprising a MAP2K6 polypeptide or nucleic acid and measuring the expression or activity of MAP2K6 in the presence or absence of the test agent to identify a candidate branching morphogenesis modulating agent and providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6, measuring the branching morphogenesis pathway in the presence or absence of the test agent, and confirming that the test agent is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

The teachings of Sodhi et al fail to cure the deficiencies of Stein et al. Sodhi et al makes no mention whatsoever of branching morphogenesis or the connection between MAP2K6 or p38 and branching morphogenesis and thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Sodhi et al.

Claims 1-6, 8, 9, 11, 17, 19, and 20 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Terada et al (Kidney International, 1999, 56:1258-1261). Claims 8, 9, 11, 17, and 19 have been canceled, rendering the rejections moot as to those claims. Applicants respectfully traverse the rejections of claims 1-6, and 20 for the reasons set forth below.

The Office indicated that Stein et al renders the claims 1-6 obvious for reasons previously stated. With respect to claim 20, the Office admitted that Stein et al do not teach or suggest an assay that measures cell cycling. However, the Office asserted that one skilled in the art would have been motivated to use such as assay based on the teachings of Terada et al, which allegedly teach that TGF-B activates the TAK-1-MKK6-p38 pathway and results in the transcriptional down-regulation of cyclin Dl.

Applicants submit that Stein et al do not teach or suggest the claimed methods for the reasons set forth previously. Specifically, Stein et al. do not teach or suggest a method comprising providing a first assay system capable of detecting MAP2K6 expression or activity comprising a MAP2K6 polypeptide or nucleic acid and measuring the expression or activity of MAP2K6 in the presence or absence of the test agent to identify a candidate branching morphogenesis modulating agent and providing a second assay system capable of detecting a change in the branching morphogenesis pathway comprising cultured cells expressing MAP2K6, measuring the branching morphogenesis pathway in the presence or absence of the test agent, and confirming that the test agent is a candidate branching morphogenesis modulating agent by detecting a change in the branching morphogenesis pathway in the presence or absence of the test agent.

The teachings of Terada et al fail to cure the deficiencies of Stein et al. Terada et al make no mention whatsoever of branching morphogenesis or the connection between MAP2K6 and branching morphogenesis and thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Terada et al.

Claims 1-6, 8-13, and 17-22 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Matsumoto et al (J. Cell Biol, 2002, 156:149-160). Claims 8-13, 17, and 19 have been canceled, rendering the rejections moot as to those claims. Applicants respectfully traverse the rejections of claims 1-6, 18, and 20-22 for the reasons set forth below.

The Office Action alleged that Stein et al. teach the MEK6 assay coupled with the p38 assay. The Office admitted that Stein et al. do not specifically teach

an assay that would measure tubulogenesis and/or apoptosis along with the cellular response to at least two different pro-angiogenic agents. However, the Office asserted that one skilled in the art would have been motivated to use such as assay based on the teachings of Matsumoto et al, which allegedly teach a link between the activation of p38 and the negative regulation of the tubulogenic response to FGF-2 and the induction of VEGF-mediated tubulogenesis without activation of p38. The Office concluded that it would have been obvious to extend the MEK6 and p38 coupled expression assays of Stein et al. to measurement of tubulogenesis and apoptosis in the response of the assay system to the pro-angiogenic agents FGF-2 and VEGF.

Applicants submit that Stein et al do not teach or suggest the claimed methods for the reasons set forth previously. The teachings of Matsumoto et al fail to cure the deficiencies of Stein et al. Matsumoto et al make no mention whatsoever of branching morphogenesis or the connection between MAP2K6 or p38 and branching morphogenesis and thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Matsumoto et al.

Claims 1-7 were rejected under 35 USC §103(a) as being allegedly obvious over Stein et al (WO 97/22704) in view of Iversen (WO 00/24885).

The Office Action alleged that Stein et al. teach that the test agent may include an antisense polynucleotide that interferes with the transcription or translation of MEK6. The Office admits that Stein et al. do not specifically teach that the antisense is a PMO. The Office alleged that Iversen et al. teaches that morphino oligonucleotides reduce the unwanted side effects related to unmodified oligonucleotides and concluded that it would have been obvious to use a PMO rather than a natural oligonucleotide as the antisense agent taught by Stein et al.

Applicants submit that Stein et al do not teach or suggest the claimed methods for the reasons set forth previously. The teachings of Iversen et al fail to cure the deficiencies of Stein et al. Iversen et al make no mention whatsoever of branching morphogenesis or the connection between MAP2K6 and branching morphogenesis and

thus fails to provide any motivation to pursue the claimed methods, much less have a reasonable expectation of success in applying them.

In view of the statements set forth above, Applicants respectfully request withdrawal of the 35 USC §103(a) rejections over Stein et al. in view of Iversen et al.

CONCLUSION

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue. If the Examiner has any questions regarding this response, she is invited to call the undersigned attorney.

Respectfully submitted,

Date: December 22, 2009

/Michelle L. McMullen-Tack /
Michelle L. McMullen-Tack, Ph.D.
Reg. No. 52,016

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, IL 60606